Please amend the application as follows:

IN THE CLAIMS:

Please cancel claims 9-10 and 24-30 as drawn to the non-elected invention.

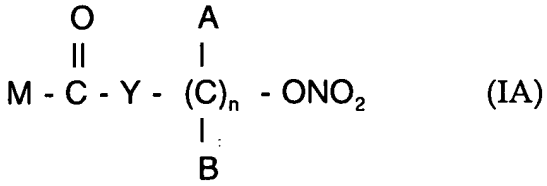
Remarks

Claims 1-8 and 19-23 are currently pending. Claims 9-10 and 23-30 have been cancelled as directed to the non-elected invention. Applicants confirm the election of Group II, drawn to a compound, composition and method of use, when the compound is structural formula (XXXI) and (XXXIII), containing napthyl and phenyl rings.

The Examiner is respectfully requested to reconsider the rejections in view of the claims and the following remarks.

I. The Claimed Invention.

Applicants' claimed invention is directed to nitric esters of derivatives of propionic acid ($Ch_3CH_2CO_2H$), claimed with the following Formula IA:



(IA)

where Y is selected from O, NH, NR_1; and where M is selected from 2-methylene-6-methoxy-naphthalene and Ch_3-CH-
|
R

where R is selected from 6-methoxy-2-napthyl-; 1-(4-*sec*butyl)-phenyl; and (cyclopentan-1-one-2-methylene)-phenyl- .

As is known, certain derivatives of propionic acid are currently marketed as anti-inflammatory agents, including 2-(6-methoxy-2-napthyl) propionic acid. (See specification, pages 2 and 3.) Unfortunately, the utilization of these propionic acid derivatives can result in severe adverse reactions to the gastrointestinal tract and damage to the liver and kidneys. (See specification at page 2, lines 14-18.) This invention is based on the discovery that nitric ester derivatives (Formual IA) of propionic acid, as defined more fully in the claims, can be used as an active pharmacological agents having anti-inflammatory and analgesic indications without the concomitant adverse side effects.

II. The Claimed Invention Is Nonobvious Over Bron, U.S. 5,049,694.

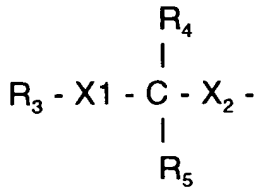
The Examiner cites Bron et al., U.S. 5,049,694, for "generically teach[ing] nitrate esters, with a structure incorporating an ester of an aromatic carboxylic acid, column 1, line 61-64, attached to an alkylene chain of 1-8 carbon atoms, which may derivatized, column 2, line 21-28, and this group terminated as a nitrate ester, column 2, line 45-50."

Applicants respectfully disagree that given the teaching of Bron et al., it would have been obvious to one having ordinary skill in the art at the time the invention was made to select a species of Bron et al. and arrive at Applicants' claimed invention.

Bron et al. teach a general formula:

$$\begin{array}{c} R_o - R_1 - (ONO_2)_n \\ | \\ R_2 \end{array}$$

where R_1 is an alkylene and the R_o substituent may be any of the following substituents: H, OH, which may be esterified by aliphatic or an (hetero)aromatic carboxylic acid or the following group (with the substituents as defined in the patent):



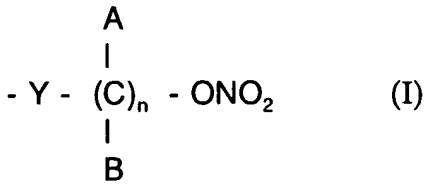
Bron et al. encompass a number of compounds, including forty-three compounds that are specifically listed in the Examples. The likelihood of arriving at Applicants' claimed compositions -- which would require a selection of the named substituents -- amounts to a hindsight selection using Applicants' disclosure as a blueprint for the selection. The fact that a claimed product is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product obvious in the absence of some directions or reasons for making such selection. There simply is no support in Bron et al. for a suggestion of the structural changes between the claimed invention and the prior art compounds. *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986); *Ex parte Krepelka*, 231 USPQ 746, 748 (BPAI 1986).

Applicants' claims define a separately patentable invention. Structural limitations in the claims cannot be ignored in determining nonobviousness. Under Section 103, the subject matter of the claimed invention, "as a whole," must be considered. There is no showing by the Examiner that Bron et al. suggests the selected substituents explicitly or implicitly because there is no suggestion contained therein.

Finally, Applicants submit that the compounds of Bron et al. are used in a different therapeutic field from that of the present invention such that any structural similarity of the Bron et al. compounds would not preclude the patentability of Applicants' claimed compounds. The Bron et al. compounds are in the field of drugs

"for the treatment of ischemiatic heart diseases (such as angina pectoris and silent ischaemia), decompensatio cordis, myocardial infarction, hypertension (in particular portal hypertension), achalasia, tardy dyskinsia, etc." (Column 1, lines 10-16.) Specifically, as disclosed in Bran et al. at Column 4, under "Pharmacology," these drugs relate to those having relaxing activity for the treamtent of heart and vascular diseases.

In contrast, the choice of substituents in Applicants' claimed nitric ester derivatives of propionic acid are optimized for their anti-inflammatory and analgesic activity, while eliminating the adverse reactions often brought about by the treatment with prior art propionic acid compounds. The problem is solved by using nitric esters of derivatives of substituted propionic acids in which the group bonded to the propionic acid is:



(I)

Bron et al. does not teach, much less suggest, that the nitro group (I), as shown above, in the substituted propionic acid would result in a compound having improved anti-inflammatory and analgesic activity.

Applicants have demonstrated in their specification at pages 22 to 27 the bioefficacy, gastrointestinal tolerance, and low toxicity of one of the elected compounds of this invention (V). Moreover, Applicants have compared their compounds with the prior art compound, 2-(6-methoxy-2-napthyl) propionic acid. Thus, Applicants' claimed compounds possess properties which render them unobvious in the pharmocologic field of anti-inflammatory and analgesic drugs.

There are structural limitations in Applicants' claims that define a separately patentable invention from Bron et al. Further, Bran et al. does not teach or suggest the compounds in the filed of anti-inflammatory and analgesic agents. Thus, considering Applicants' claimed invention "as a whole," Bron et al. do not suggest the selected substituents explicitly or implicitly and the claimed invention is nonobvious. The Examiner therefore is respectfully requested to reconsider this rejection under Section 103 and to withdraw it.

III. Conclusion.

Applicants respectfully submit that all the basis for rejection have been overcome by the above remarks. Reconsideration of the application is respectfully requested. It is believed that this application is now in condition for allowance. The Examiner is invited to contact the undersigned on any questions that might arise.

Respectfully submitted,

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